REMARKS

Applicants respectfully request entry of the above amendments to Claim 24. Claims 16-18 and 24 are pending.

Claim 24 has been amended to more clearly indicate the subject matter of the claim, and to place the claims in condition for allowance or in better form for appeal. The amendments to Claim 24 find support, for example, in Claim 15 as originally filed, and in the specification at page 3, lines 3-5; page 10, lines 14-15; page 11, lines 29-39 to page 12, lines 1-6; page 29, lines 25-30; page 30, lines 10-17; and elsewhere in the specification and claims as originally filed.

No new matter is added by way of the claim amendments.

Previous Rejections and Present Status of the Claims

A response was filed to the final Office Action dated June 30, 2004. The amendments in that response were entered. In the Advisory Action mailed September 27, 2004, the Examiner noted that the priority date of the application is February 7, 1997 and that some of the rejections made in the Office Action of June 30, 2004 have been withdrawn. However, two claim rejections were maintained. The remaining claim rejections are:

Claims 16, 17, and 24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sodhi et al., *Biochemistry and Molecular Biology International* **35**:559-565 (1995). In Section 10 of the Office Action dated June 30, 2004 (reiterated in the Advisory Action of September 27, 2004), the Examiner stated "Sodhi et al. teaches the use of anti-phosphotyrosine-FITC antibody, a fluorescently labeled and detectable antibody, to study proteins. It is an inherent property of the prior art antibody to specifically bind tyrosine-phosphorylated proteins. In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds to an epitope contained within the protein of SEQ ID NO: 1."

Claims 16-18 and 24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Frackleton et al., *Journal of Biological Chemistry* **259**:7909-7915 (1984).

In Section 11 of the Office Action dated June 30, 2004 (reiterated in the Advisory Action of September 27, 2004), the Examiner stated "Frackelton et al. teaches the use of an anti-phosphotyrosine monoclonal antibody, which is produced by a hybridoma cell line, to isolate proteins. It is an inherent property of the prior art antibody to specifically bind tyrosine-phosphorylated proteins. In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds to an epitope contained within the protein of SEQ ID NO: 1."

Applicants respectfully traverse the rejections to the claims for at least the reasons discussed below.

In order to better understand the present situation with regard to the pending antibody claims and to provide a comprehensive perspective regarding Applicants' traversal of the present rejections of the antibody claims, Applicants present a brief synopsis of the previous claim amendments and of the rejections made to them by the Examiner. For brevity, this synopsis focuses on the independent antibody claim (initially Claim 15, then Claim 24) from which the other claims depend; however, it will be understood that amendments and related arguments directed to the other claims were also made. Finally, the arguments relating to the pending rejections over Sodhi and Frackelton are directly addressed in the final section of the remarks below.

Thus, in the following remarks, Section I discusses the prosecution history of the pending application, and Section II discusses the pending rejections and presents arguments in favor of the allowance of all pending claims.

I. A Summary of the Prosecution History of the Independent Antibody Claims

The present application is directed to antibodies to novel polypeptides. Applicants have discovered novel polypeptides, as acknowledged by the issuance of United States patents to these novel polypeptides in related cases (*e.g.,* U.S. Patent No. 6,111,073 to polypeptides and U.S. Patent No. 6,040,437 to nucleotides encoding such polypeptides). It is well accepted that antibodies to novel polypeptides are patentable subject matter, as acknowledged by numerous issued United States patents

directed to such subject matter. However, despite repeated rewriting of claim language in response to repeated rejections by the Examiner, applicants have been unable to obtain allowance of claims directed to the novel antibodies of the invention.

The present application has a long prosecution history, which is summarized below. Throughout the prosecution of this application, Applicants have been very considerate of the concerns of the Examiner. Throughout the prosecution history of this case, Applicants have gone out of their way to try to address the Examiner's concerns about the scope of the claims and his concerns about alleged anticipation that might result from such concerns. The sole purpose for the claim amendments made throughout the prosecution of this application has been to advance the claims to allowance in view of the Examiner's concerns. However, as has been apparent throughout the prosecution, and as indicated below, the Examiner's reading of the original claim language and the prior art has been unreasonable.

After more than five years of failed attempts to satisfy such unreasonable rejections, Applicants believe it is time to return closely to the original claim language, which is, and has always been clearly distinguishable over the prior art.

The Present Application

The present application is a Request for Continued Examination of U.S. Patent Application No. 09/068,377, filed May 8, 1999, which claims priority under 35 U.S.C. §371 to PCT US98/01774, filed January 30, 1998, and to prior U.S. Patent Application Nos. 08/938,830, filed September 29, 1997 (now U.S. Patent No. 6,040,437) and 09/798,419, filed February 7, 1997. Thus, the earliest priority date for the present application is February 7, 1997.

The original independent antibody claim was original Claim 15:

"15. An antibody capable of specific binding to the PSTPIP polypeptide of Claim 1."

This claim referred to original Claim 1, which was:

"1. An isolated PSTPIP polypeptide selected from the group consisting of:

(i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO: 1);

(ii) a polypeptide having at least 65% sequence homology with the PSTPIP amino acid sequence of Fig. 1A (SEQ ID NO: 1); and

(iii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid encoding the polypeptide of (i);

provided that the polypeptides of (ii) and (iii) substantially retain the ability to bind a member of the PEST-type protein tyrosine phosphatases."

The Amendment of April 7, 2000

Following a Restriction Requirement mailed on March 8, 2000, Claim 15 was amended to include the language of Claim 1, as follows:

"15. An antibody capable of specific binding to a PST phosphatase interacting protein (PSTPIP) polypeptide selected from the group consisting of:

(i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO: 1); and

(ii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to the complement of nucleic acid of SEQ ID NO: 2 said polypeptide substantially retaining the ability to bind to a protein tyrosine phosphatase which (a) possesses a non-catalytic domain comprising a region rich in proline, serine and threonine residues and a C-terminal 20 amino acid segment which is rich in proline residues, and (b) defines at least one SH3 binding domain wherein said stringent conditions are hybridization in a solution containing 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6-8), 0.1% sodium pyrophosphate, 5x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% sodium dodecyl sulfate (SDS) and 10% dextran sulfate at 42°C in 0.2 x SSC and 0.1% SDS."

In an Office Action issued November 7, 2000, Claims 15-18 and 22 (directed to antibodies capable of specific binding to a PST phosphatase interacting protein

(PSTPIP) polypeptide) were rejected: under 35 U.S.C. §112, first paragraph; under 35 U.S.C. §112, second paragraph; under 35 U.S.C. §102(b) as allegedly anticipated by Sodhi, Frackelton, and other references; and under 35 U.S.C. §103(a) as allegedly obvious over some named references. The grounds of rejection alleged by the Examiner included, for example, that the PSTPIP allegedly acts "via physiological mechanisms that are not understood" (page 11, line 20); that, since the PSTPIP is an intracellular protein, allegedly "the integrity of a cell membrane would necessarily have to be disrupted in order to contact PSTPIP with an antibody" (page 12, lines 20-22); and that the claims were allegedly indefinite "because Claims 15 and 22 recite the term 'substantially'"(page 19, lines 4-5).

With respect to the rejections for alleged anticipation by the cited references, the Examiner suggested that "it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds PSTPIP" (Office Action dated November 7, 2000, page 20, lines 6-7). However, it should be noted that neither of the antibodies of Sodhi and Frackelton (anti-phosphotyrosine-FITC and anti-phosphotyrosine, respectively) were raised against PSTPIP polypeptide antigens. Other references cited in other rejections discussed antibodies that were raised against, *e.g.,* FLAG sequences, and yeast GAL4 transactivating protein (the nucleotide encoding that protein apparently has nucleotide homologies to the 5' untranslated regions of the PSTPIP nucleotide sequence, but the protein itself has no polypeptide homology with the PSTPIP polypeptide). Thus, none of the cited references provide antibodies raised against PSTPIP polypeptides or that specifically bind to PSTPIP polypeptides.

The Amendment of January 23, 2001

An Amendment was mailed on January 23, 2001 in response to the Office Action dated November 7, 2000. Claim 15 was amended to recite: "An antibody capable of specific binding to a polypeptide epitope of a PSTIP selected from the group ...," to delete the word "substantially" that had been objected to by the Examiner, and to add

the phrase "followed by wash at 42°C" in response to the Examiner's objection that no wash step had been specified in the claim.

Claim 15 thus became:

"15. An antibody capable of specific binding to a polypeptide epitope of a PST phosphatase interacting protein (PSTPIP) polypeptide selected from the group consisting of:

(i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO: 1); and

(ii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to the complement of nucleic acid of SEQ ID NO: 2 said polypeptide ~~substantially~~ retaining the ability to bind to a protein tyrosine phosphatase which (a) possesses a non-catalytic domain comprising a region rich in proline, serine and threonine residues and a C-terminal 20 amino acid segment which is rich in proline residues, and (b) defines at least one SH3 binding domain wherein said stringent conditions are hybridization in a solution containing 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6-8), 0.1% sodium pyrophosphate, 5x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% sodium dodecyl sulfate (SDS) and 10% dextran sulfate at 42°C followed by wash at 42°C in 0.2 x SSC and 0.1% SDS."

In a final Office Action dated March 21, 2001, the Examiner's previous rejections under 35 U.S.C. §101 and under 35 U.S.C. §112, second paragraph, were withdrawn; and rejections under 35 U.S.C. §112, first paragraph, were maintained, as were rejections under 35 U.S.C. §102.

Although the Examiner stated: "The examiner agrees with Applicant's statement that the GAL4 gene does not encode any part of the amino acid sequence of SEQ ID NO:1" (Office action mailed March 21, 2001, page 18, lines 1-2), the 35 U.S.C. §102(b) rejection over Parthun (which discusses the GAL4 gene) was maintained. The Examiner apparently felt that the GAL4 protein sequence might somehow be expressed when the PSTPIP polypeptide was expressed, stating "There is no evidence in the

record that the nucleotide sequence of SEQ ID NO: 2 encoding the GAL4 protein is contained within the 5'-untranslated region of the polynucleotide encoding the PSTPIP polypeptide comprising the amino acid sequence identified in SEQ ID NO: 1." (Office action mailed March 21, 2001, page 17, lines 18-21.) The Examiner did not explain how the fact that "the GAL4 gene does not encode any part of the amino acid sequence of SEQ ID NO:1" was not evidence in the record that the GAL4 protein was not expressed when the PSTPIP polypeptide was expressed.

The Examiner also remarked that "[t]here is no evidence in the record that proves that a fusion protein comprising the GAL4 protein and the PSTPIP polypeptide is not expressed" (Office action mailed March 21, 2001, page 17, lines 29-30), although the Examiner agreed, as noted above, that the "GAL4 gene does not encode any part of the amino acid sequence of SEQ ID NO:1" (*i.e.,* that SEQ ID NO: 1 does not include GAL4 sequence). Thus, the claims remained rejected although no cited reference discussed the amino acid sequence of SEQ ID NO:1 nor antibodies to it.

The Amendment of September 18, 2001

In a Preliminary Amendment accompanying a Request for Continued Examination, following an Amendment After Final (mailed July 6, 2001), pursuant to an Advisory action mailed August 22, 2001 and in response to the final Office Action dated March 21, 2001, Claim 15 was amended as follows:

"15. An antibody that binds specifically ~~capable of specific binding~~ to ~~a polypeptide epitope of~~ a PST phosphatase interacting protein (PSTPIP) polypeptide sequence within a polypeptide selected from the group consisting of:

(i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO: 1); and

(ii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to the complement of nucleic acid residues 682 to 1926 of SEQ ID NO: 2, said stringent conditions comprising hybridization in a solution containing 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate

(pH 6-8), 0.1% sodium pyrophosphate, 5x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% sodium dodecyl sulfate (SDS) and 10% dextran sulfate at 42°C followed by wash at 42°C in 0.2 x SSC and 0.1% SDS, and which has both ~~said polypeptide retaining~~ the ability to stimulate actin polymerization and the ability to bind to a protein tyrosine phosphatase which (a) possesses a non-catalytic domain comprising a region rich in proline, serine and threonine residues and a C-terminal 20 amino acid segment which is rich in proline residues, and (b) defines at least one SH3 binding domain ~~wherein said stringent conditions are hybridization in a solution containing 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6-8), 0.1% sodium pyrophosphate, 5x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% sodium dodecyl sulfate (SDS) and 10% dextran sulfate at 42°C followed by wash at 42°C in 0.2 x SSC and 0.1% SDS~~."

In addition, a new Claim 23 was added which was directed to an assay for identifying a cell membrane permeable antagonist or agonist antibody of a PSTPIP polypeptide.

In the Office Action dated November 21, 2001, the pending claims were rejected and were subjected to restriction.

Although the pending claims recited specific SEQ ID NO:s, and although the Examiner acknowledged that "the claimed subject matter of the parent application" which issued in co-owned U.S. Patent No. 6,111,073 by the one of present inventors "also encompasses the genus of PSTPIP molecules to which the claimed antibodies of the instant application must bind" (see the Office Action dated November 21, 2001, page 6, lines 8-11), the antibody claims of the present application were again rejected under various theories.

For example, despite the claim limitations of 1) a single polypeptide sequence (SEQ ID NO: 1) and 2) a single polynucleotide sequence (SEQ ID NO: 2) in Claim 15, the Examiner felt that "it is not clear from the disclosure that Applicants describe more than one species of PSTPIP" (Office Action dated November 21, 2001, page 6, lines 11-12) and that it "perhaps only includes adequate description of a single species

of the genus of PSTPIP molecules" (Office Action dated November 21, 2001, page 6, lines 12-14). The Examiner apparently felt that there was "need to provide a written description of a more reasonable number of the members of the ... claimed genus of antibodies that bind specifically to the various and different members of the genus of PSTPIP molecules" (Office Action dated November 21, 2001, page 6, lines 15-19).

In addition, the Examiner felt that naming specific nucleic acids of a sequence introduced a "negative limitation," stating: "Furthermore, it is noted that the recitation of "a polypeptide encoded by nucleic acid residues 682 to 1926 of SEQ ID NO:2 " appears to be a negative limitation since it excludes polypeptides encoded by nucleic acid molecules that hybridize under stringent conditions to the complement of other portions of SEQ ID NO:2." (Office Action dated November 21, 2001, page 10, lines 6-10). The Examiner also objected to the phrase "an antibody that binds specifically to a PST phosphatase interacting protein (PSTPIP) sequence *within* a polypeptide" (italics added by the Examiner) as allegedly lacking antecedent basis. (Office Action dated November 21, 2001, page 10, lines 14-17.)

In this regard, the Examiner also noted that the definition of the term PSTPIP included the word "comprises" and stated that PSTPIP polypeptides thus included fusion proteins (Office Action dated November 21, 2001, page 10, lines 30-31). Thus, the Examiner reasoned that "amending Claim 15 to recite "[a]n antibody that binds specifically to a PST phosphatase interacting protein (PSTPIP) sequence within a polypeptide" appears to direct the claim to a subgenus of antibodies, and that this subgenus was not described by the original disclosure of the genus of antibodies that bind specifically to a PSTPIP polypeptide comprising the amino acid sequence of SEQ ID NO: 1." (Office Action dated November 21, 2001, page 11, lines 7-12.)

Although some previous rejections were withdrawn in this Office Action, the claims were again rejected as anticipated by Sodhi and Frackelton, neither of which disclose a PSTPIP polypeptide or antibodies directed to such a polypeptide, and were rejected as obvious over several references.

The Amendment of February 21, 2002

In response to the Office Action dated November 21, 2001, Claims 15 and 23 were canceled and a new Claim 24 was added:

"24. An antibody that binds to the PST phosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO: 1 at a site not including a phosphorylated tyrosine, within said SEQ ID NO: 1."

Applicants noted in this response that the antibodies of Sodhi and of Frackelton would not bind to the PSTPIP polypeptide sequence of SEQ ID NO: 1 other than at a phosphorylated tyrosine.

In an Office Action mailed August 27, 2002, the Examiner rejected new Claim 24, again suggesting that the claims were allegedly directed to a subgenus of antibodies not described by the original disclosure of the genus of antibodies that bind a PSTPIP polypeptide comprising the amino acid sequence of SEQ ID NO: 1 (Office Action of August 27, 2002, page 7, line 7-9). In addition, the Examiner suggested that "the phrase 'at a site not including a phosphorylated tyrosine' is a negative limitation since it is intended to exclude anti-phosphotyrosine antibodies that bind the polypeptide of SEQ ID NO: 1." (Office Action of August 27, 2002, page 7, line 12-14).

Thus, although the Examiner noted that "the claims are drawn to an antibody that binds the polypeptide of SEQ ID NO: 1" (Office Action of August 27, 2002, page 4, lines 27-28), that the reference polynucleotide would reasonably encode a polypeptide (page 4, lines 28-29), and explicitly stated that "Applicants have correctly noted that the primary reference does not teach the polynucleotide sequence of SEQ ID NO:2" (Office Action of August 27, 2002, page 5, lines 23-24), the Examiner rejected the claims as obvious over the cited reference.

The Amendment of June 26, 2003

In response to the Office Action dated August 27, 2002, Claim 24 was amended to recite:

"24. An antibody that binds to the PST phosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO: 1 at a site not including a phosphorylated tyrosine ~~within said SEQ ID NO: 1~~ of said polypeptide."

In an Office Action mailed September 8, 2003, the claims were rejected by the Examiner on several alleged grounds. Many of the references were dated after the presently acknowledged priority date of the application, so that these rejections need not be discussed in this review.

The Examiner objected to the phrase "at a site not including a phosphorylated tyrosine of said polypeptide," suggesting that there was insufficient antecedent basis for this limitation (Office Action of September 8, 2003, page 4, lines 22-24). The Examiner again suggested that this language, although amended to remove "*within*" that had previously been objected to, was directed to a subgenus of antibodies not adequately described in the specification (Office Action of September 8, 2003, page 5, lines 4-9). The also again suggested that the phrase "at a site not including a phosphorylated tyrosine" was a negative limitation (Office Action of September 8, 2003, page 5, lines 10-15).

The Amendment of December 18, 2003

In response to the Office Action dated September 8, 2003, Claim 24 was amended to recite:

"24. An antibody derivable from an antibody-producing cell from an animal that has been immunized with a PSTphosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO: 1 that specifically binds to an epitope within SEQ ID NO: 1 of the ~~PST phosphatase interacting protein (~~PSTPIP~~)~~ polypeptide of SEQ ID NO: 1 ~~at a site not including a phosphorylated tyrosine of said polypeptide~~."

This amendment removed the language "at a site not including a phosphorylated tyrosine of said polypeptide" that had been objected to by the Examiner.

In the Office Action dated June 30, 2004, this claim was rejected on the grounds that it allegedly was not supported by the specification as originally filed. Regarding the phrase "derivable from an antibody-producing cell," the Examiner was concerned that allegedly "the only example of the selected antibody producing cells are lymphocytes" (Office Action of June 30, 2004, page 3, lines 16-17). Regarding the phrase " an epitope within SEQ ID NO: 1 of the PSTPIP polypeptide of SEQ ID NO: 1" the Examiner was concerned that the specification allegedly "does not describe an epitope within the polypeptide of SEQ ID NO: 1" (Office Action of June 30, 2004, page 3, line 20). In addition, the claims were rejected on other alleged grounds, including alleged anticipation by Sodhi and Frackelton.

The Amendment of September 3, 2004

In response to the Office Action dated June 30, 2004, Claim 24 was amended to recite:

"24. An antibody derivable from ~~an antibody-producing cell~~ a lymphocyte from an animal that has been immunized with a PSTPIP polypeptide of SEQ ID NO:1 or fragment thereof that specifically binds to ~~an epitope within SEQ ID NO:1 of the~~ a PSTPIP of SEQ ID NO: 1."

The amended claim no longer included the phrase "antibody-producing cell" that had been objected to, but instead recited "a lymphocyte," which had been acknowledged by the Examiner as an antibody-producing cell that was disclosed in the specification. The amended claim no longer included the phrase "an epitope within SEQ ID NO: 1" that had been objected to, but instead recited that the claimed antibody "specifically binds to a PSTPIP of SEQ ID NO: 1."

In response to the Amendment of September 3, 2004, an Advisory Action was issued, in which it was noted that the priority issue had been resolved, with the earliest priority date of Claims 16-18 and 24 being February 7, 1997, and many rejections from the Office Action of June 30, 2004 were withdrawn. However, as noted above,

Claims 16-18 and 24 remain rejected in the Advisory Action dated September 27, 2004 as allegedly anticipated under 35 U.S.C. §102(b) by Sodhi and Frackelton.

Comments on the Prosecution History

In numerous amendments over a five-year-long prosecution, Applicants have attempted to present claims directed to antibodies to a novel polypeptide. The novelty of the polypeptide has been acknowledged by the Examiner and by the United States Patent and Trademark Office (*e.g.,* see U.S. Patent Nos. 6,040,437 (nucleotide sequence) and 6,111,073 (polypeptide sequence)). However, each attempt to claim the invention in language acceptable to the Examiner's concerns was met with further quibbles and rejections over language that would be clear to any practitioner of the art to which the present invention pertains.

As noted above, the rejections included rejections on the alleged grounds that "the PSTPIP allegedly acts 'via physiological mechanisms that are not understood'"; that naming specific nucleic acids of a sequence introduced a "negative limitation"; that the phrase "an antibody that binds specifically to a ... PSTPIP... sequence *within* a polypeptide" was found objectionable; that although the Examiner explicitly stated that "Applicants have correctly noted that the primary reference does not teach the polynucleotide sequence of SEQ ID NO:2", the Examiner rejected the claims as obvious over the cited reference; among other rejections.

In addition, the claims remain rejected as allegedly anticipate by references that do not disclose the polypeptides to which the claimed antibodies specifically bind (which polypeptides may or may not be phosphorylated), presumably because the Examiner believes that "It is an inherent property of the prior art antibody to specifically bind tyrosine-phosphorylated proteins." The Examiner has not, however, explained how an antibody that recognizes any phospho-tyrosine on any polypeptide can be said to specifically bind to a PSTPIP polypeptide of SEQ ID NO:1 or to anticipate an antibody that is raised against and does specifically bind to a PSTPIP polypeptide of SEQ ID NO:1.

Applicants respectfully note that some might characterize this unremitting series of rejections as "unreasonable."

In addition, it appear that the rejections are inconsistent with USPTO examinations in other cases. For example, recently issued U.S. Patent No. 6,559,285 (examined by Examiner Stephen L. Rawlings) includes the following independent claim:

1. An isolated antibody or isolated fragment thereof which antibody or fragment immunospecifically binds to a lats protein, which lats protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, and SEQ ID NO: 8.

The specification of this patent discloses that a lats protein may be phosphorylated (*e.g.,* column 20, line 33). However, antibodies to phosphorylated serine residues are known, as indicated, for example, by Kono et al., "Anti-phosphoserine and anti-phosphothreonine antibodies modulate autophosphorylation of the insulin receptor but not EGF receptor" *Biochem Biophys Res Commun* **196**:216-222 (1993), which was published before the priority date of U.S. Patent No. 6,559,285.

In spite of the fact that the prior art disclosed phosphoserine antibodies, claims were allowed directed to antibodies against a protein that may be phosphorylated at serine or other residues. This is a reasonable result, since the prior art anti-phosphoserine antibodies were not raised against the novel lats polypeptide of U.S. Patent No. 6,559,285. However, this result is <u>not</u> consistent with the rejections of analogous claims in the present application.

Applicants respectfully submit that claim rejections, to be supportable, should be reasonable and should be consistent with the examination of analogous claims in other cases.

II. <u>Arguments Regarding the Present Rejections under 35 U.S.C. § 102(b)</u>

In the present Preliminary Amendment, claim 24 stands amended to recite:

"24. (currently amended) An antibody ~~derivable from a lymphocyte from an animal that has been immunized with~~ <u>that specifically binds to</u> a PST phosphatase

interacting protein (PSTPIP) polypeptide of SEQ ID NO:1 ~~or fragment thereof that specifically binds to a PSTPIP polypeptide of SEQ ID NO:1~~."

Thus, currently pending Claim 24, written in clean form, recites "An antibody that specifically binds to a PST phosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO:1."

Applicants again note that a PST phosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO:1 is novel, and is not found in the cited references.

The Rejection of Claims 16, 17, and 24 Under 35 U.S.C. §102(b) over Sodhi

Claims 16, 17, and 24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sodhi et al., *Biochemistry and Molecular Biology International* **35**:559-565 (1995).

Anticipation under 35 U.S.C. §102 requires that "every element of the claimed invention be identically shown in a single reference." (*In re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990).

Sodhi is presented as discussing the use of an anti-phosphotyrosine-FITC antibody, a fluorescently labeled and detectable antibody, to study proteins. The Examiner states: "It is an inherent property of the prior art antibody to specifically bind tyrosine-phosphorylated proteins. In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds to an epitope contained within the protein of SEQ ID NO: 1."

However, Sodhi fails to discuss a PSTPIP polypeptide of SEQ ID NO: 1 and fails to discuss an antibody to a PSTPIP polypeptide of SEQ ID NO: 1.

Applicants submit that an anti-phosphotyrosine-FITC antibody does not specifically bind to a PSTPIP polypeptide of SEQ ID NO: 1. As is clear from the Examiner's discussion of such an antibody, an anti-phosphotyrosine-FITC antibody will bind any protein or polypeptide having a phosphotyrosine. In that an anti-phosphotyrosine-FITC antibody will bind any polypeptide having a phosphotyrosine, such an antibody is not specific to a particular tyrosine-phosphorylated protein or

polypeptide. In particular, such an antibody does not specifically bind a PSTPIP polypeptide of SEQ ID NO: 1.

In addition, an anti-phosphotyrosine-FITC antibody will not bind a protein or polypeptide that does not have a phosphotryosine. The specification discloses that the PSTPIP may be either non-phosporylated or phospohorylated. For example, a PSTPIP polypeptide may be dephosphorylated by a phosphatase (*e.g.,* at page 42, lines 1-19 and Fig. 6). An anti-phosphotyrosine-FITC antibody will not bind a PSTPIP polypeptide that is not phosphorylated. In that a PSTPIP polypeptide need not be phosphorylated, an anti-phosphotyrosine-FITC antibody will often not bind to a PSTPIP polypeptide. This would not be true of an antibody that specifically binds a PSTPIP polypeptide.

Thus, for at least the reasons that the anti-phosphotyrosine-FITC antibody of Sodhi is not specific to a PSTPIP polypeptide of SEQ ID NO: 1, and that in many cases will not bind at all to a PSTPIP polypeptide of SEQ ID NO: 1, the anti-phosphotyrosine-FITC antibody of Sodhi does not specifically bind to a PSTPIP polypeptide. Accordingly, Sodhi fails to anticipate the present invention. Applicants respectfully submit that the rejections of Claims 16, 17, and 24 under 35 U.S.C. §102(b) as allegedly anticipated by Sodhi are overcome.

The Rejection of Claims 16-18 and 24 Under 35 U.S.C. §102(b) over Frackleton

Claims 16-18 and 24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Frackleton et al., *Journal of Biological Chemistry* **259**:7909-7915 (1984). Claims 16-18, and amended Claim 24 require, among other elements, that the claimed antibody specifically bind to a PST phosphatase interacting protein (PSTPIP) polypeptide of SEQ ID NO:1.

Frackelton is presented as discussing the use of an anti-phosphotyrosine monoclonal antibody to isolate proteins. The Examiner stated "Frackelton et al. teaches the use of an anti-phosphotyrosine monoclonal antibody, which is produced by a hybridoma cell line, to isolate proteins. It is an inherent property of the prior art antibody to specifically bind tyrosine-phosphorylated proteins. In light of the

specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds to an epitope contained within the protein of SEQ ID NO: 1."

However, Frackelton fails to discuss a PSTPIP polypeptide of SEQ ID NO: 1 and fails to discuss an antibody to a PSTPIP polypeptide of SEQ ID NO: 1.

Applicants submit that an anti-phosphotyrosine monoclonal antibody does not specifically bind to a PSTPIP polypeptide of SEQ ID NO: 1. As discussed above, and as is clear from the Examiner's discussion of such an antibody, an anti-phosphotyrosine monoclonal antibody will bind any protein or polypeptide having a phosphotyrosine, and so is not specific to a particular tyrosine-phosphorylated protein or polypeptide. In particular, an anti-phosphotyrosine monoclonal antibody does not specifically bind a PSTPIP polypeptide of SEQ ID NO: 1.

In addition, an anti-phosphotyrosine monoclonal antibody will not bind a protein or polypeptide that does not have a phosphotryosine. As discussed above, the specification discloses that a PSTPIP polypeptide may be non-phosphorylated. An anti-phosphotyrosine monoclonal antibody will not bind a PSTPIP polypeptide that is not phosphorylated. Thus, since a PSTPIP polypeptide may not be phosphorylated, an anti-phosphotyrosine-FITC antibody will often not bind to a PSTPIP polypeptide. This would not be true of an antibody that specifically binds a PSTPIP polypeptide.

Thus, for at least the reasons that the anti-phosphotyrosine monoclonal antibody of Frackelton is not specific to a PSTPIP polypeptide of SEQ ID NO: 1, and that in many cases will not bind at all to a PSTPIP polypeptide of SEQ ID NO: 1, the anti-phosphotyrosine monoclonal antibody of Frackelton does not specifically bind to a PSTPIP polypeptide of SEQ ID NO: 1. Accordingly, Frackelton fails to anticipate the present invention. Applicants respectfully submit that the rejections of Claims 16-18 and 24 under 35 U.S.C. §102(b) as allegedly anticipated by Frackelton are overcome.

CONCLUSION

The claim amendments are believed to place the claims in condition for allowance or in better form for appeal. Reconsideration and allowance of all pending claims is respectfully requested. All claims being believed to be in *prima facie* condition for allowance, an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641**, referencing Attorney's Docket No. **39766-0061 CP2**.

Respectfully submitted,

Date: October 29, 2004

By: _____
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